

TRANSMITTAL FORM

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 Filing Date: November 1, 2001
 First Named Inventor: Robert H. Broyles
 Art Unit: 1632
 Examiner Name: Janice Li Qian

Total Number of Pages in this Submission : _____

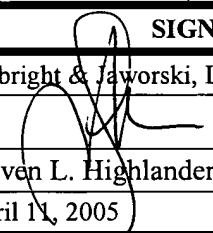
Attorney Docket Number: OMRP:027US

ENCLOSURES (check all that apply)

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<input checked="" type="checkbox"/> Declaration of Dr. Robert H. Broyles
<u>Under 37 C.F.R. § 1.132</u> |
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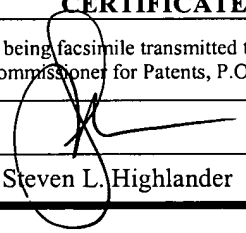
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Printed Name	Steven L. Highlander	Reg. No.	37,642
Date	April 11, 2005		

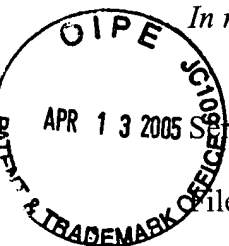
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Typed or Printed Name	Steven L. Highlander	Date	April 11, 2005

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re Application of:
Broyles *et al.*

Serial No.: 10/003,669

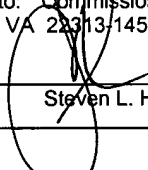
Filed: November 1, 2001

For: GENE REGULATION THERAPY
INVOLVING FERRITIN

Group Art Unit: 1632

Examiner: Janice Li Qian

Atty. Dkt. No.: OMRf:027US/SLH

CERTIFICATE OF MAILING 37 C.F.R. § 1.8	
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April 11, 2005 Date	 Steven L. Highlander

DECLARATION OF DR. ROBERT H. BROYLES UNDER 37 C.F.R. §1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

I, the undersigned, do declare that:

1. I am a citizen of the United States. I am a named inventor on the above-captioned application. I currently hold the position of Professor in the Department of Biochemistry & Molecular Biology at Oklahoma University Health Science Center, and Research Member, in the Free Radical Biology & Aging Research Program at the Oklahoma Medical Research Foundation. A copy of my *curriculum vitae* is attached.

2. In FIG. A (attached), we present a Western blot and an associated bar graph that show induction of the endogenous FtH gene in human cells (NT-2 cells) by abscissic acid added to the medium for 8 days. We have also found this induction of FtH by the same compound in human K562 cells (not shown).
3. In FIG. B (attached), we show initial data from a transgenic mouse made to express human FtH in definitive erythroid cells that are elaborated by the fetal liver beginning in mid-gestation. These red blood cells are the first to express the adult beta-globin genes of the mouse, and the construct in which we inserted the FtH gene was made to direct expression of FtH only in these cells and at the same time as the adult mouse beta-globin. The strain of mouse from which these initial data were collected has *two* types of adult beta-globin genes, beta-major (which accounts for 60% of the expression) and beta-minor (40%). The *key* to this experiment is that *only* the beta-major globin gene of the mouse has the CAGTGC DNA motif that is the core of the FtH binding site; the beta-minor globin gene lacks this site. Thus, when the human FtH transgene is activated in the definitive mouse red cells, the expression of the mouse beta-major globin gene will be repressed but the beta-minor gene will *not* be repressed because it lacks the FtH repression site. So, the transgenic mice will be expected to be born alive but have a reduced beta-major/beta-minor ratio and a mild beta-thalassemia due to excess alpha-globin chains (because the mouse has no fetal globin gene to up-regulate in place of beta-major). The presence of "target cells" (red blood cells with a dark spot in the center) in the blood smear of these transgenics and the reduced beta-major/beta-minor ratio seen

the UT-PAGE globin gel constitute evidence that human FtH can function as a beta-globin gene repressor in a living animal.

4. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

March 8, 2005
Date

Robert H. Broyles
Robert H. Broyles, Ph.D.

CURRICULUM VITAE

Robert H. Broyles, Ph.D.

**Professor of Biochemistry & Molecular Biology
The University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma**



Personal Data

Date of birth: 2/16/43

Place of birth: Kingsport, Tennessee
Broyles

S.S. Number: 233-68-6864

Family: Wife: Dianne Fields

Children: David, b. 1/21/75
James, b. 2/10/77

Addresses: Dept. of Biochemistry &
Molecular Biology
Univ. of Oklahoma Health Sciences Center

Telephones: (405)271-2227, ext. 1213
or ext. 1215
FAX: 405/271-3092

212 NW 20th Street
Oklahoma City, OK 73103

(405)525-5802

Educational Background

B.S., 1965

(in chemistry; minor in physics and mathematics) (advisor, Dr. P.J. Hamrick)

Wake Forest College

Winston-Salem, North Carolina

Embryology Course, summer, 1969

(with Dr. Malcolm Steinberg)

Marine Biological Laboratory

Woods Hole, Massachusetts

Ph.D., 1970

(with Dr. C. F. Strittmatter)

(in biochemistry; minor in microbiology and physiology)

Title of dissertation: Development and Characteristics of Glucose-6-phosphate
and 6-Phosphogluconate Dehydrogenases in the Sea Urchin and the Frog.

Dept. of Biochemistry, The Bowman Gray School of Medicine
of Wake Forest University, Winston-Salem, North Carolina

Postdoctoral, 1970-72

(with Dr. Earl Frieden)

(biochemistry of amphibian metamorphosis)

Dept. of Chemistry, Florida State University
Tallahassee, Florida

Professional Experience

Research Assistant (with Dr. R.W. Cowgill) Dept. of Biochemistry Bowman Gray School of Medicine Winston-Salem, North Carolina	summer, 1966
Research Associate, Dept. of Chemistry Florida State University Tallahassee, Florida	1970-1972
Assistant Professor, Department of Zoology, Univ. of Wisconsin-Milwaukee	1972-1977
Member of the Graduate Faculty, Univ. of Wisconsin-Milwaukee	1972-1977
Member, Center for Great Lakes Studies, Univ. of Wisconsin	1975-1977
Tenure approved, UW-Milwaukee	1977
Associate Professor, Department of Biochemistry and Molecular Biology, College of Medicine Univ. of Oklahoma Health Sciences Center	1977-1985
Associate Professor of Dental Biochemistry College of Dentistry Univ. of Oklahoma Health Sciences Center	1977-
Member of the Graduate Faculty, University of Oklahoma	1977-present
Tenured, University of Oklahoma	1979
Professor of Biochemistry and Molecular Biology University of Oklahoma Health Sciences Center	1985-
Adjunct Professor, Department of Pediatrics University of Oklahoma College of Medicine	1988-

Senior Scientist, National Institutes of Health, NIDDK, Division of Kidney, Urologic and Hematologic Diseases	1989, 1990
Guest Worker, National Institutes of Health, NIDDK, Laboratory of Chemical Biology	1989-94; 1995-97
Assistant Director, M.D./Ph.D. Program, College of Medicine, University of Oklahoma	1991-99
Visiting Scientist, Free Radical Biology & Aging Research, Oklahoma Medical Research Foundation	1999-2001
Research Member, Free Radical Biology & Aging Research, Oklahoma Medical Research Foundation	2001-

Other Experience

Invited Participant, 6th Workshop on Molecular Techniques for
Developmental Biologists, sponsored by the National Science
Foundation, at the University of California, San Diego, July
2-28, 1973.

Lecturer, Embryology Course, Marine Biological Laboratory, Woods
Hole, Massachusetts, August, 1983.

Sabbatical, Marine Biological Laboratory, Woods Hole,
Massachusetts, 6/83 - 11/83.

Invited Participant, Gordon Conference on Red Cells, Plymouth State
College, Plymouth, New Hampshire, 1985, 1987, 1989.

Invited Speaker, International Conference on *New Trends in the Treatment of
Hemoglobinopathies and Thalassemias*, Paris, France, September 8-12, 1994.

Invited Session Chair, 10th NIH Conference on Hemoglobin Switching, 1996

Invited Participant, NIH Hemoglobin Switching Conferences, Airlie House, Virginia, &
University of Washington, Seattle/Rosario Resort, Orcas Island, WA, 1978,
1980, 1982, 1984, 1986, 1988, 1990, 1992, 1994, 1996, 2000, **2004**.

Invited Participant/Presenter, 13th NIH Conference on Hemoglobin Switching, St. John's

College, Oxford, England, September 11, 2002.

Professional Societies

American Association for the Advancement of Science, 1965-present
 American Association of Laboratory Animal Science, 1987
American Association for Cancer Research, 2003-
 American Chemical Society, 1966-1972
 American Society of Biological Chemists/Amer.Soc.Biochem. & Molecular Biol., 1985-2005
 American Society for Cell Biology, 1977-1999
 American Society of Gene Therapy, 1998-2005
 American Society of Hematology, 1986-present
 American Society for Microbiology, 1986-1988
 American Society of Zoologists, 1971-1994
International BioIron Society (IBIS), 2003-
 International Society of Differentiation, 2000-
 New York Academy of Sciences, 1978-1980: 1990-1992
 Oklahoma Academy of Sciences, 1981-1982
 Oxygen Society, 2000-2001 [became SFBM, below]
 Society for Developmental Biologists, 1973-present
 Society for Experimental Biology and Medicine, 1978-1980
Society for Free Radical Biology & Medicine, 2001-
 Society of Sigma Xi, 1973-present; chapter Pres.-elect, 1988-89, 1990-91; Chapter President, 1991-92; Past Pres., 1992-93.

Awards and Honors

(See list of Patents and Research Grants Received, below.)

Honorary Scholarship, Wake Forest College	1961-1963
Honorary Fraternities (undergraduate), chemistry and mathematics	1963-1965
NDEA Title IV Predoctoral Fellowship	1965-1968
Wilder Fellowship, Bowman Gray School of Medicine	1968-1970
NIH Postdoctoral Fellowship (Individual NRSA)	1970-1972
Elected to Sigma Xi (Marquette Chapter)	1973
Nominee, Aesculapian Award (for teaching), College of Medicine, Univ. of Oklahoma Health Sciences Center	1979
Distinguished Service Award, Dept. of Bioc. & Mol. Biol., Univ. of Oklahoma Health Sciences Center	1982
Elected to membership, American Society of Biological Chemists	1985
Elected to membership, American Society of Hematology	1986
MASUA (Mid-America State Universities Association)	1988-89
Honor Lecturer	(continued)

Awards and Honors (continued)

Elected to membership, American Association for Cancer Research	2003
Elected to membership, International BioIron Society	2003

Honorary Biographical Listings:

American Men & Women of Science, 19th Edition
Who's Who in the South and Southwest, 24th Edition
Who's Who in American Education, 5th Edition
Who's Who in the World, 13th Edition
Who's Who in Science and Engineering, 2nd Edition
Intrntl. Directory of Distinguished Leadership, 6th Ed.(nominated)
Men of Achievement, 17th Edition (nominated)

Member, NIH Council/Study Sections/Site Visit Teams:

NCI, Study Section Member, RFA for Marine/Freshwater Models for Carcinogenesis	1986
NIDDK, DKUHD, SBIR Grants, Internal Review Committee	1989
NIDDK, DKUHD, Conference Grants Review Committee	1989, 1990
NIDDK, National Advisory Council, Program Representative, DKUHD	1989, 1990
NHLBI, Sickle Cell Center Site Visit Team	March, 1992
NHLBI, Sickle Cell Center Site Visit Team	April, 1992
NHLBI, Sickle Cell Center Site Visit Team	May, 1992
NHLBI, Study Section Member, RFA on Gene Therapy for Sickle Cell Disease	June, 1994
NHLBI, Study Section (Ad hoc), Training Grant Review	Oct., 1994
NHLBI, Study Section (Ad hoc), Training Grant Rev.	May, 1995
NHLBI, Study Section Member, Gene Therapy for Sickle Cell Disease, Program Projects	June, 1995
NHLBI, Study Section Member, RFA on Sickle Cell Disease Treatments,	June, 1996
NHLBI, Special Emphasis Panel, Comprehensive Sickle Cell Centers	May, 1997

Current Research Interests

Regulation of gene expression during development
(particularly, developmental hemoglobin switching)

Sickle Cell Disease: molecular approaches to treatments

Role of iron-binding proteins in gene regulation

Carcinogenesis in vitro (especially, hepatocarcinogenesis
studied with liver organ cultures)

Use of the natural iron chelator, Ferritin-H, in treating neurodegenerative diseases

“Back-Burner” Research Interests (can be reactivated):

Model systems in developing amphibians (embryos, larvae, organ explant cultures)

Effects of environmental pollutants (e.g., PCBs, polychlorinated
biphenyls) on development and birth defects

Current Teaching Interests

Molecular biology (e.g., regulation of gene expression)

Molecular basis, diagnosis & proposed treatment of genetic diseases

Molecular & cellular basis of new biotechnologies

Cellular differentiation and carcinogenesis

Developmental biology and birth defects

General biochemistry, general biology, cell biology

History of Scientific Thought in Biochemistry and Molecular Biology

Current Interests in Administration

To stimulate and encourage research collaborations among scientists
and physicians with related interests

To help encourage the use of a variety of extramural funding
mechanisms for research

To encourage and promote interdisciplinary approaches to education and research

Patents Pending

1. **Broyles, R.H.**, and Floyd, R.A. "*Gene Regulation Therapy Involving Ferritin*" U.S. Patent Applic. Ser. No. 60/245,003 (Pending).
2. **Broyles, R.H.**, and Floyd, R.A., "*Gene Regulation Therapy Involving Ferritin.*" European PA No. 01992721.9 (Pending).
3. **Broyles, R.H.**, Roth, A.C., Floyd, R.A., and Belegu, V. "*Abscissic Acid and Derivatives Thereof for the Treatment of Diseases.*" U.S. Provisional Patent Application OMRF:067USP1) written for submission.

Research Grants Awarded (Principal Investigator on all)

	<u>dates</u>	<u>agencies</u>	<u>titles</u>
1.	1970-1972	NIH, NHLBI (Indiv. NRSA)	Regulation of globin mRNA synthesis during metamorphosis
2.	1973-1977	Research Corporation (Cottrell Grant)	Effect of thyroid hormones on the metamorphic hemoglobin transition.
3.	1974-1975	Grad.Coll., UW-Milw.	Effects of the larval lampricide TFM on red blood cell differentiation in the sea lamprey <u>Petromyzon marinus</u> .
4.	1975	Center for Great Lakes	Effects of the lampricide TFM (3-trifluoro-methyl-4-nitrophenol) UW-Mil. Studies, on hemoglobin synthesis by the sea lamprey and other species.
5.	1975-1976	NOAA (U.S. Sea Grant Program)	Effects of polychlorinated biphenyls on the early development of white fish.
6.	1975-1976	Grad. Coll., UW-Milw.	TFM, an inhibitor of hemoglobin synthesis: How does it work in sea lamprey, and does it do the same thing to Great Lakes fishes?
7.	1976-1977	NOAA (U.S. Sea Grant Program)	Effects of PCBs & other chlorinated hydrocarbons on the early development of lake trout and other Great Lake fishes.
8.	1976-1977	NIH/NIAMDD (R01)	Differentiation of red blood cells <u>in vitro</u> .

At OUHSC

9.	1977-1979	NIH/NIAMDD (R01)	Differentiation of red blood cells <u>in vitro</u> .
10.	1977-1978	OUHSC Coll. of Med. Small Grant	Regulation of hemoglobin synthesis in red blood cells differentiating <u>in vitro</u> .
11.	1979-1983	NIH/NIAMDD (R01)	Regulation of hemoglobin switching <u>in vivo</u> and <u>in vitro</u> .
		(Competitive continuation of above, retitled/expanded w/ suppl. funds)	
12.	1981	OUHSC Research Council	An <u>in vitro</u> approach to studying hepatocarcinogenesis.
13.	1982-1983	OU Associates Fund	Cloning of a set of developmentally-regulated genes: A tool for deciphering gene control mechanisms.
14.	1983-1988	NIH/NIADDDK NIDDK (R01) (2nd competitive continuation)	Regulation of Hb switching in vivo and <u>in vitro</u> .
15.	1986-1988	Presbyterian Hlth.Fndtn. PHF	Regulation of Hemoglobin Switching <u>In vivo</u> and <u>In vitro</u> .
16.	1988-1989		Regulation of Hemoglobin Switching <u>In vivo</u> and <u>In vitro</u> .
17.	1989-1990	NIH/NIDDK	Contract (IPA), with NIDDK, Div. of Kidney, Urologic & Hematologic Diseases (90% of salary/FB)
18.	7/91-10/92	PHF Seed Grant	Silencing Sickle Cell: A Repressor of the Human Beta Globin Gene
19.	5/92-4/93	Provost's Postdoct. Fellowship Award	for Dr. Biji T. Kurien, Madras Univ., as matching funds to PHF Seed Grant
20.	9/96-8/98	Pres.Hlth.Fndtn. (funded)	"Advances in Human Molecular Genetics" (Distinguished Lecturer Series and Graduate Course)
21.	9/98-8/2000	Pres.Hlth.Fndtn. (funded - Compet. Continuation)	"Advances in Human Molecular Genetics" (Distinguished Lecturer Series and Graduate Course)
22.	02/01/01-01/31/06	NIH/NCI	R01: "Free Radicals and Choline-deficient Liver Carcinogenesis" 5 R01 CA082506 Co-Investigator (Subcontract)
23.	02/01/02-01/31/05	NIH/NCI	R01 Supplement: "Organotypic Liver Cultures and Hepatocarcinogenesis" 3 R01 CA082506-02S1
24.	07/01/01-06/30/03	AHA/OK Affil.	Predocctoral Fellowship for Visar Belegu "Elucidation of the Function and Regulation of

Ferritin in Atherosclerotic Lesions." PI
Invited Presentations

<u>Date</u>	<u>Institution/location/society</u>
1. Mar.,1972	Zoology, Univ.of Wisconsin-Milwaukee
2. Feb.,1973	Biochemistry, Medical College of Wisconsin
3. Apr.,1974	17th International Conference on Great Lakes Research, Hamilton, Ontario
4. June,1975	Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC
5. Nov.,1975	Biology, Carroll College, Waukesha, WI
6. Nov.,1976	Biochemistry and Molecular Biology, Univ. of Oklahoma Hlth. Sci. Ctr.
7. Mar.,1977	20th International Conference on Great Lakes Research, Ann Arbor, MI
8. Mar.,1978	ICN-UCLA Symposium, Hemopoietic Cell Differentiation, Keystone, Colorado
9. June,1978	1st NIH Conference on Hemoglobin Switching, Battelle Institute, Seattle, WA
10. Apr.,1979	Biochemistry, Texas Tech Univ. School of Medicine, Lubbock
11. Nov.,1979	Noble Foundation, Biomedical Branch, Ardmore, Oklahoma
12. Mar.,1980	Developmental Biology Group, Dept. of Zoology, Univ. of Texas at Austin
13. June,1980	2nd NIH Conference on Hemoglobin Switching, Airlie House, Virginia
14. Feb.,1981	Biology, Pennsylvania State Univ., University Park, PA
15. Mar.,1981	Oklahoma Medical Research Foundation, Oklahoma City
16. July,1982	Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC
17. Sept.,1982	3rd NIH Conference on Hemoglobin Switching, Rosario Resort, Orcas Is., WA
18. Oct.,1982	Anatomical Sciences, Univ. of Oklahoma Health Sciences Center, Oklahoma City
19. Nov.,1982	Immunology Discussion Group (Drs. Paul Kincaid and Robert A. Good), Oklahoma Medical Research Foundation (OMRF), Oklahoma City
20. Aug.,1983	Embryology Course, Marine Biological Laboratory, Woods Hole, Massachusetts
21. Oct.,1983	Hematology, Dept. of Medicine, Harvard Med.Sch., Brigham & Women's Hospitals, Boston, MA
22. Oct.,1983	Biology, Mt. Holyoke College, South Hadley, MA
23. Nov.,1983	Biological Sciences Division, Univ. of Connecticut, Storrs
24. Oct.,1984	4th NIH Conference on Hemoglobin Switching, Airlie House, Virginia
25. Aug.,1985	Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH
26. Nov.,1985	Anatomical Sciences, Univ. of Oklahoma Health Sciences Center, Oklahoma City
27. Dec.,1985	Biochemistry & Molecular Biology, OUHSC
28. Dec.,1985	Hematology Section, Dept. of Medicine, OUHSC
29. Sept.,1986	Biological Sciences, Texas A & M Univ., College Station
30. Oct.,1986	5th NIH Conference on Hemoglobin Switching, Airlie House, Virginia
31. Oct.,1986	Zoology, Univ. of Oklahoma, Norman

32. Oct.,1986 Mid-America Molecular Biology Colloquium, OUHSC, Shangri-La Rst., Afton, OK
33. Nov.,1986 Biochemistry & Molecular Biology, OUHSC
34. Aug.,1987 Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH
35. Sept.,1987 Physiology & Biophysics, OUHSC
36. Oct.,1987 2nd Mid-America Molecular Biology Colloquium, OUHSC, Waterford Hotel, Oklahoma City
37. Feb.,1988 Hematology/Oncology, Dept. of Medicine, OUHSC
38. Feb.,1988 Biomedical Research Symposium, Presbyterian Health Foundation, Oklahoma City (platform presentation)
39. Mar.,1988 National Institutes of Health, NIDDK, Div. of Kidney,Urologic & Hematologic Diseases, Bethesda, MD
40. Sept.,1988 6th NIH Conference on Hemoglobin Switching, Airlie House, Virginia
41. 1988-89 MASUA (Mid-America State Universities Association) Honor Lecturer. Presentations on Developmental Regulation of Globin Genes.
42. Nov.,1988 Depts. of Anatomy and Biochemistry, Univ. of Nebraska Med. Ctr., Omaha
43. Apr.,1989 Anatomy and Cell Biology, Univ. of Kansas Med. 4Ctr., Kansas City
44. Apr.,1989 Genetics Section, Dept. of Medicine, Johns Hopkins Univ. School of Medicine, Baltimore
45. May, 1989 Laboratory of Chemical Biology, NIDDK, NIH, Bethesda, MD
46. Aug.,1989 Gordon Conference on Red Cells, Plymouth State College, Plymouth, NH
47. Oct.,1989 Biochemistry, Bowman Gray School of Medicine, Wake Forest Univ., Winston-Salem, NC (In honor of the retirement of Dr. C.F.Strittmatter)
48. June,1990 7th NIH Conference on Hemoglobin Switching, Airlie House, Virginia
49. Mar.,1992 Lady Davis Institute for Medical Research, McGill University, Montreal, Quebec
50. June,1992 8th NIH Conference on Hemoglobin Switching, Rosario Resrt, Orcas Is., WA
51. July,1992 Pediatrics, Univ. of Maryland at Baltimore
52. Nov.,1992 Laboratory of Chemical Biology, NIDDK, National Institutes of Hlth, Bethesda, MD
53. Feb.,1993 Genetics, Endocrinology and Metabolism Sections, Dept. of Pediatrics, OUHSC
54. Mar.,1993 Biology, Univ. of Tulsa, Tulsa, Oklahoma
55. Nov.,1993 Biochemistry & Molecular Biology, OUHSC
56. June,1994 9th NIH Conference on Hemoglobin Switching, Rosario Resrt, Orcas Is.,WA
57. Sept.,1994 INSERM/NIH/WHO/Conference on Sickle Cell Disease & Thalassemias, Paris, France
58. Nov.,1994 Biochemistry, Oklahoma State Univ., Stillwater
59. Jan.,1995 Physiology & Biophysics, OUHSC
60. Sept.,1995 Grand Rounds, Dept. of Pediatrics, OUHSC
61. June,1996 10th NIH Conf. on Hemoglobin Switching, Orcas Is., WA
62. Nov.,1996 Molec.& Cell.Biol.Prgm, Arizona State U., Tempe
63. Dec.,1996 Biochem.& Molec.Biol., Coll. of Med., OUHSC

- 64. Oct., 1998 11th NIH Conf. on Hemoglobin Switching, Orcas Is., WA
- 65. Nov., 1998 Free Radical Biol. & Aging Section, Oklahoma Medical Research Foundation
- 66. June, 2000 12th NIH Conf. on Hemoglobin Switching, Orcas Is., WA
- 67. Nov., 2000 Oxygen Society, San Diego, CA (platform presentation)
- 68. Dec., 2000 Free Radical Biology & Aging Section, Okla. Med. Res. Foundation
- 69. **Feb., 2001 Biochemistry & Molecular Biology, Coll. Of Med., OUHSC**
- 70. **Nov., 2001 Soc. Free Rad. Biol. & Med., Res. Triangle Park, NC (oral presentation)**
- 71. **Sept., 2002 13th NIH Conf. on Hemoglobin Switching, Oxford, England**
- 72. **Sept., 2004 14th NIH Conf. On Hemoglobin Switching, Orcas Island, WA**
- 73. **Feb., 2005 Free Radical Biology & Aging Section, Oklahoma Medical Res. Fndtn.**

Selected Research Accomplishments
(shared with students and collaborators)

First to demonstrate and identify a repressor for the human β -globin gene, the gene mutated in sickle cell disease and to suggest use of gene repression as a phenotypic cure for this genetic disease (with Visar Belegu, Sandeep Shah, Charles Stewart, Quentin Pye, Robert A. Floyd and others)

Proc. Natl. Acad. Sci., USA 98, 9145-9150 (2001),

First to demonstrate DNA looping between different parts of a gene promoter using a restriction enzyme and EMSA (electromotive shift assay) (with Bijl T. Kurien, Dana Stewart and others)

FASEB J. 8, A1272/#80 (1994).

FASEB J. 9 (6), A1328 (1995).

Sickle Cell Disease & Thalassaemias: New Trends in Therapy 234,43-51 (1995).

Devel. Biol. 175 (#2), 380 (1996).

Blood 88 (#10), 23b (1996).

Discovered a new, human DNA-binding protein with unique properties which is a candidate repressor of the adult beta globin gene, has properties of a ferritin subunit, and binds an important upstream control region of DNA that contains an iron response element (IRE) consensus sequence (with Dana R. Stewart, Fred Blair, Kim Kyker and others)

Blood 76 (#10, suppl. 1), 56a (1990).

FASEB J. 6 (1), A72, #411 (1992).

FASEB J. 9 (6), A1328 (1995).

Sickle Cell Disease & Thalassaemias: New Trends in Therapy 234,43-51, (1995).

First to show that trans-acting factors that mediate development of globin gene switching are conserved between mammals and amphibians, using erythroid heterokaryons formed in vitro (with Janet Barker, David Smith, Larry Ramseyer, Robert Jarman and other students)

Blood 66, 126a (1985); Fed. Proc. 45, 1577 (1986); Blood 68, 138a (1986); J. Cell Biol. 105, 320a (1987); J. Cell Biol. 107, 98a (1989).

Prog. Clin. Biol. Res. 251, 285-294 (1987).

Exptl. Cell Res. 178, 435-448 (1989).

Prog. Clin. Biol. Res. 316 B, 83-96 (1989).

Devel. Biol. 133, 262-271 (1989).

Devel. Genetics 15, 347-355 (1994).

Molecular Biology of Hemoglobin Switching Chap. 26, pp. 313-329 (1995).
Sem. Cell Devel. Biol. 10, 259-265 (1999).

First to clone and sequence a globin cDNA from the bullfrog, *Rana catesbeiana*. (with David J. Smith, Bruce A. Roe, and Austin F. Riggs)

Blood 68, 138a (1986); J.Cell Biol.105, 320a (1987); J.Cell Biol.107, 98a (1989).
J.Biol.Chem.268, 26961-26971 (1993)..

First to report successful cultures of adult rat liver as a long-term organ culture. (with Martin J.Griffin and Virginia I Stark-Vancs)

Cancer Letters 38, 347-358, 1988.

Delineated the red cell populations and erythropoietic microenvironments involved in developmental hemoglobin switches for the entire life cycle of the bullfrog *Rana catesbeiana*. (with graduate and medical students)

Nature New Biol. 241, 471-474 (1973).
Science 190, 471-473 (1975).
Devel.Biol. 81, 299-314 (1981).
Proc.Natl.Acad.Sci.,USA 79, 5592-5596 (1982).
Devel.Biol. 96, 515-519 (1983).
In Hematopoiesis: A Developmental Approach (L.I. Zon, ed.) Oxford Univ. Press (2001).

Discovered that the failure of lake trout to reproduce in Lake Michigan is likely due to PCB contamination, which kills the young at a crucial developmental stage. (with graduate student Martin I. Noveck)

Toxicol.Appl.Pharmacol. 50, 291-298 (1979).
Toxicol. Appl.Pharmacol. 50, 299-308 (1979).

Research Students Mentored

<u>Ph.D. Students</u>	<u>degree date</u>	<u>Honors, subsequent appts.</u>
1. Visar Belegu (co-advisor)	2004	AHA Predoc Fellowship; Postdoc, John W. McDonald, Johns Hopkins Univ.
2. Christina Bourne (co-avisor)	2003	Postdoc, Adam Zlotnick
3. David J. Smith	1990	Capt. U.S. Army
4. Phillip B. Maples	1984	Postdoc, E.Goldwasser Res. VP, Baxter Hlth.Care
5. Allan R. Dorn	1982	Postdoc, Robert Good Fndr/Pres.,SeptraTek Res.Sctst, SeraDyne
 <u>M.D. Students</u>		
6. Sandeep Shah	2002	Presb/Harris Schlr, 1999
7. Frederick Blair	1997	Presb/Harris Schlr, 1992
8. Anna M. Likos	1995	Presb/Harris Schlr, 1992
9. Donna Sexton Jackson	1990	Presb/Harris Schlr, 1988 March of Dimes Schlr,1988
10. Lorenz T.H. Ramseyer	1989	Presb/Harris Schlr,1986,1987 March of Dimes Schlr,1986
11. Robert N. Jarman	1989	Presb/Harris Schlr, 1987
12. Virginia Stark-Vancs	1987	March of Dimes Schlr, 1984 NIH/HHMR Schlr,1985-86 Intern/Res,Georgetown,1987-89 Fellow/Sr. Invest, NCI, 1989-96 Member, Texas Cancer Care, 1996-98 Arlington Cancer Ctr./ Director of Clinical Research, Harris Methodist Oncol.

13. Gary R. Kindell	1984	Intern/Res, UT-SW, Dallas
<u>M.S. Students</u>		
14. Fredrick Blair	1996 (pend.)	M.D., OUHSC
15. Kimberly D.Kyker	1995	
16. Donna Sexton	1987	M.D., OUHSC
David J. Smith	1985	Ph.D., OUHSC
Phillip B. Maples	1981	Ph.D., OUHSC
17. Allan R. Dorn,	1979 (Zool.)	UW- Milwaukee
	1977	Ph.D., OUHSC
18. Gary R. Kostlan	1977, UW-Milw.	Dir.,Qual.Cont.,Borden
19. Keith C. Meyer	1977, UW-Milw.	M.D., UW-Madison
20. Martin I. Noveck	1977, UW-Milw.	M.D., UW-Madison
21. Martin F. Messar	1977, UW-Milw.	Chair,Sci.Dept.,Luck,WI
22. William J. Saucier	1976, UW-Milw.	M.D., UW-Madison
23. Michael J. Deutsch	1974, UW-Milw.	Astra Pharmaceuticals
<u>Undergraduates</u>		
24. Rebecca Ceraig-Schapiro	2004-2005	Honors Thesis, OU; nom. Rhodes Scholar
25. Austin C. Roth	2003, 2004	Univ. of Mass., Amherst
26. Katharine M. Harris	2004	Univ. of Mass., Amherst
27. Anthony Haney	1995	OU Med.Sch., 1996
28. Dana R. Stewart	1991-93	Univ.Central OK
29. Kari A. McBride	1987-88	Central State Univ
30. Gerda Breitwieser	1977	UW-Milw; Ph.D., Wash.U.;
		Postdoc, UT-Galveston;
		Asst/Assoc. Prof.,
		Johns Hopkins Univ.
31. Stuart Berger	1975	M.D.,UW; faculty, UW
32. Richard Reid	1974	B.A., UW-Milw.
33. Gintaris Dargis	1974-76	B.A., UW-Milw.
34. Harry Whelan	1973-77	B.A., UW-Milw.,
		M.D., UW; faculty, Vanderbilt
<u>High School Students</u>		
35. Austin Roth	1999-2000	Classen Sch. Adv. Studies
36. Mairead Todd	1998	Classen Sch. Adv. Studies,
		Oklahoma City
37. Ashley Sides	1995	High Sch., Drumright,OK
		Ntl.Merit Scholar, OU-Norman
38. Jada Benn	1993-4	Notre Dame Univ.
39. Thuy H. Do	1986	B.S., Purdue Univ.

40. Kari A. McBride	1985-87	B.S.,Nursing, Emory
41. Sherris A. Harris	1987, 1988	N.E. High Sch., OKC
42. Ha Do	1988	N.E. High Sch., OKC
43. Melba Moore (Jr. High Sch.)	1984	N.E. High Sch., OKC

Teaching Experience

Approximately 14,000 students taught, 1972-2004.

<u>Courses taught</u>	<u>Years</u>	<u>University</u>
*Animal Biology (Zool.101,lect/lab)	1972-76	UW-Milwaukee
Biology of Man (Biol.102,guest lect.)	1974-76	UW-Milwaukee
History of Biology (Bot.414, one lect.)	1973	UW-Milwaukee
Embryology (Zool.360, guest lect.)	1973	UW-Milwaukee
**Pblms in Developmental Biol.(Biol.420)	1974-76	UW-Milwaukee
**Cell Biology (Zool.211/lect. & lab.)	1976	UW-Milwaukee
**Cell Physiology (Zool.470/lect. & lab)	1973-77	UW-Milwaukee
Undergrad.Seminar in Biol.(Zool. 670)	1972-73	UW-Milwaukee
**Independ. Study, Undergrad.(Zool. 699)	1973-77	UW-Milwaukee
**Adv. Independ. Study, Grad.(Zool, 899)	1973-77	UW-Milwaukee
*Biology Colloquium (Zool. 900)	1973	UW-Milwaukee
**Adv. Gene Regulation (Zool, 925)	1973	UW-Milwaukee
**Cell Differentiation (Zool. 925)	1974	UW-Milwaukee
**Nobel Prizes,Cell/Molec.Biol.(Zool.925)	1977	UW-Milwaukee
**Molec./Cell.Aspects, Develop.(Zool.926)	1973	UW-Milwaukee
*Research (Zool. 990)	1973-77	UW-Milwaukee
Intro.Biochem.(BIOC 4104)	1977-86	OUHSC
*MSI Biochemistry	1977-82,1984-98	OUHSC
MS Review Course in Biochemistry	1978-81	OUHSC
MSI, Medical Molecular Genetics	1996-2004	OUHSC
*Clinical Correlations(sickle cell disease)	1991-2004	OUHSC
*Clinical Correlations (carcinogenesis)	1979	OUHSC
Dental Biochemistry	1977-82,1984-88	OUHSC
Gen.Biochem.,grad.students(BIOC 5215/8)	1979-95	OUHSC
Biochem. Lab (BIOC 5224)	1986-88;1992-96	OUHSC
Molecular Biol.& Genetics(BIOC/MI 5243)	1991-98	OUHSC
*Grad. Seminar (BIOC 5971/5970)	1977-99	OUHSC
*Adv. Biochem. Lab (BIOC 6224)	1979-94;1996	OUHSC
Human Biochemical Genetics(BIOC 6244)	1979-82	OUHSC
Molecular Oncology(BIOC 6312)	1977-78	OUHSC
*Cell Biology (BIOC 6223)	1986-88,1992-99	OUHSC
**Adv.Topics,Human Molec.Genetics(BIOC 6205)	1993-99	OUHSC

Macromolec.Struct.& Fnctn.(BIOC 6215/6214)	1980-82,92-98	OUHSC
*Molec.Biol.& Biochem. Genetics(BIOC 6235/6234)	1977-1999	OUHSC
*Research/Doctoral Dissert.(BIOC 6980)	1977- 2004	OUHSC
*Spec.Pblms.Biochem.(BIOC 6990)	1979,1987-88,1994-98	OUHSC
*Spec.Studies,Med. Students(BIOC/MED 9980)	1984-88;92	OUHSC
Transcriptional Regulation (BIOC 6340)	2004-2005	OUHSC

*Team-taught courses coordinated one or more times.

**Courses designed, coordinated and taught.

Selected Accomplishments in Teaching and Education

Originator and Coordinator of a graduate course entitled "Advanced Topics in Human Molecular Genetics" (from 1993), which utilizes 12-15 distinguished guest lecturers recognized as leaders in this area

This is an upper-level graduate seminar-discussion course utilizing a combination of local faculty and nationally recognized experts in current molecular approaches to human diseases. A different topic is considered each week, fifteen topics per semester. The format is two class meetings per week, the first being a student discussion of papers from the current literature led by local faculty, and the second consisting of a lecture by an invited expert in the area being considered. After this public lecture, the students spend an hour sequestered with the guest speaker in a relaxed atmosphere discussing items of mutual interest. The guest faculty have included **13 Nobel Laureates** and **35 members of the National Academy of Sciences**, and all speakers are distinguished in their fields. To our knowledge, this is the best seminar series in molecular biology in the U.S.A. and the best course of its kind in the world.

Research Mentor/Advisor to thirty-nine students at various levels (1975-2001), all of whom have made significant progress and contributions to science at levels beyond their training, including:

Ph.D Student, Alan R. Dorn (Ph.D., 1982), who subsequently did a postdoc with National Academy of Sciences member Robert Good, and was later creator, founder, and president of SeptraTek, Inc., the first biotechnology company in Oklahoma City, which successfully marketed a unique one-step clinical procedure for quickly obtaining pure human mononuclear leukocytes from whole blood (under product trade name SeptraCell-MN). Dr. Dorn is a Research Director with Seradyne.

M.D. Student, Virginia I. Stark-Vancs (M.D., 1987), who was accepted for the first class of 24 NIH/Howard Hughes Medical Research Scholars (1985-86) and spent a year in the laboratory of gene therapy pioneer Dr. French Anderson (the "father" of gene therapy), as a member of his "gene team." Dr. Stark-Vancs earned the M.D. from OUHSC in 1987, did a residency in internal medicine at Georgetown University, and was a Clinical Research Fellow at the National Cancer Institute, National Institutes of Health, Bethesda, Maryland, from 1991-96. She is currently an oncologist with Texas Cancer Care in Fort Worth.

M.S. Student, Gary R. Kostlan (M.S., 1977), became Director of Quality Control, Cultured Products, for Borden Dairy, Milwaukee, Wisconsin, the nation's largest dairy. He has continued to progress in the dairy industry.

B.S. Student, Gerda Breitwieser (B.S., 1977), went on to a Ph.D. at Washington University in St. Louis, a postdoc at Galveston, and an Assistant Professor, Department of Physiology, Johns Hopkins University School of Medicine, Baltimore. She was recently promoted to Associate Professor with tenure.

High School Student, Thuy H. Do (1986), won third place in biology with his research project in the International Science Fair in Puerto Rico. He subsequently obtained B.S. degree and a commission in the U.S. Navy, from Purdue University.

Originator of Graduate Seminars and Courses in:

- Cell Physiology with laboratory (1973)
- Molecular & Cellular Aspects of Development (1973)
- Cellular Differentiation (1974)
- Advances in Gene Regulation (1975)
- Cell Biology (1976)
- Nobel Prizes in Cellular & Molecular Biology (1977)

Advanced Topics in Human Molecular Genetics (1993 - 1999)

Nominated for an Aesculapian Teaching Award (1979) by the medical student class of 1982.

Taught approximately 14,000 students (1972-2005).

Administrative Experience/University Service

Department of Zoology Committees, UW-Milwaukee:

- Course and Curriculum	1973-75
- Electron Microscope Committee	1973-77
- Capital Equipment	1972-73,1975-76
- Ph.D. Program Proposal Committee	1972-75
- Zoology 101 Course Committee	1972-76
- Graduate Affairs Committee	1972-73
- Biology Colloquim	1973-74
- Faculty Salary Committee	1976-77
- Public Relations	1976-77
Instnl.Review Brd.Protectn.Human Subjects, UW-Milw.	1975-77
Dean's Facul.Advis.Comm.,Coll.of Letters & Sci.,UW-Milw	1974-77
Graduate Course Comm.,Grad.Coll.,UW-Milw	1973-75
Search Committee for a Microbiologist, UW-Milw	1973-75
Microbiology Prgm Planning Comm., UW-Milw	1974-75
Faculty Senate UW-Milw	1973-75
# Committee, Jnt Grad. Studies, UW-Milw/Med.Coll.Wis.	1973-76
# Biol. Sciences Ph.D. Prgm Steering Comm., UW-Milw.	1975-77
# Joint Course & Curric. Comm.,Zool/Bot, UW-Milw	1973-74
# Amer. Soc. Zoologists, Campus Rep. UW-Milw	1975-77

Dept. of Biochem.& Molec.Biol.Committees, OUHSC:

# - Biochemistry and Molecular Biology Seminar	1987-88
# - Search Committee for Biochem.Faculty (3)	1984-85
- Search Committee for Molecular Biologist	1984-85
# - Search Committee for Molecular Biologist (1)	1982
- Department Head's Advisory Committee	1978-79
# - Graduate Admissions and Recruitment	1977-83,1992
# - Qualifications Comm.for Biochem.Grad.Facul.	1985-87
- Tenure/Promotions/Joint Appointments Comm.	1979-80;81-83
# - Comm.to Formulate Guidelines,Tenure/Promotions	1979-80
# - BIOC 6235 Course Committee	1981-83,1978-87
# - BIOC 6223 Course Committee	1991-92
# - BIOC 6502 Course Committee (<u>Chair</u>)	1991-99
- BioTech MS Degree Task Force	1995-97
# - General Exam Comm.	1978-79,1981-82,1986-88,1992-93,1995-2002
- Joint Faculty Review & Evaluation Committee	1995-2005
# - Fred & Marie Gray Research Award Comm.(<u>Chair</u>)	1992-2003

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|---|---|--------------------|
| # | - Graduate Student Travel Awards Comm. (<u>Chair</u>) | 1996-2003 |
| | - Graduate Student Awards Committee | 2004-2005 |
| # | - MS I Biochem. Course Committee | 1977-81; 1984-2005 |

College and University-wide Committees

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|---|--|-----------------|
| # | Res. & Sci. Affairs Comm., Faculty Senate OUHSC | 1982-84 |
| # | Scientific Merit Subcomm., Amer. Heart Assoc., OK Affil. | 1978-83 |
| | Amer. Heart Assoc., OK Affiliate, Res. Policy Comm. | 1980-83 |
| | Search Committee, Dir. of Animal Resources & Facilities | 1984-85 |
| | IACUC (Institutional Animal Care & Use Committee) | 1984-88 |
| | Research Council OUHSC | 1982 (declined) |
| | Graduate Council OUHSC | 1981-84 |
| # | Grad. Coll. Curric. Comm. OUHSC | 1992-94 |
| # | Interdisciplinary Pgm Steering Comm. OUHSC | 1992-94 |
| | Faculty Senate (Alternate), Coll. of Med. OUHSC | 1991-94 |
| | Graduate Education Research Day (GERD): | |
| | - Prize Paper Committee | 1979-80 |
| | - Judge, Basic Sciences | 1992 |
| | Facul. Adviser, Coll. of Med. Grad. Stu. Assoc. OUHSC | 1991-96 |
| | MD/PhD Prgm. Steering Comm., Coll. of Med. OUHSC | 1991-99 |
| # | Faculty Appeals Board OUHSC/University | 1981-82/1995-99 |

Committees chaired one or more years.

Selected Accomplishments in Administration and Service

Assistant Director, MD/PhD Program, College of Medicine (1991-99)

Encouraged/advised three Native American students to apply for NIH Minority Predoctoral Fellowships from NIGMS and conferred with the NIGMS Program Officer by telephone numerous times. All three applications were funded; one of our students had the highest ranked application in the country. Mentored three students through their first two years of the program. Created a new course in human genetics for MD/PhD and PhD students that brings Nobel Laureates, National Academy members, and other distinguished scientists to campus to meet with these students.

Chair, Search Committee for Faculty in Biochemistry & Molecular Biology (1982, 1984-85)

Wrote advertisements, recruited candidates, and guided the review and ranking of the candidates, which led to short lists of nationally-competitive scientists and the hiring of five outstanding faculty members. Our ad drew over 100 fine applicants.

Member, Search Committee for Director of Animal Resources (1984-85)

The top candidate we recommended was hired - Dr. Gary White, now one of the top animal resources directors in the country.

Chair, Research & Scientific Affairs Committee, Faculty Senate, OUHSC (1982-84)

Recommended to the Provost that the number of research awards for faculty be increased beyond the one available at that time (i.e., the GLC Professorship). This recommendation was transmitted through the Faculty Senate, approved, and instituted as the Provost's Research Awards. This inducement helped double the extramural research funding over a five-year period (1981-1986).

Chair, General Examination Committee, Department of Biochemistry & Molecular Biology (1978-79, 1981-82, 1986-88, 1992-97; member, 1997-99; 2000- 2002).

In 1986-88, designed and instituted the format used for 8 years for the General Examination for Admission to Ph.D. Candidacy in Biochemistry and Molecular Biology, which was uniformly endorsed and favored by department faculty. The Exam included two days of written comprehensive tests in biochemistry and molecular biology, a written research proposal in the form of an NIH RO1 grant application, and an oral exam covering both the comprehensive knowledge and research proposal sections. This was among the most rigorous prelim exams in the country and highly valued by students, for three reasons: (1) In studying for the comprehensive portions, the students found that they organized and integrated everything that they had learned. They made a comprehensive set of notes, gained a thorough overview of biochemistry and molecular biology, and saw interrelationships they had not seen before. (2) They learned a very practical skill - how to write a research grant proposal - and had that skill evaluated by successful investigators. (3) Upon successfully completing the exam,

students say that they felt a great sense of accomplishment as well as a marked increase in self-confidence about their ability to teach, to do research, or to do both.

In 1998, a new format was designed that was overwhelmingly accepted by the Graduate Program Faculty. The students now write a research proposal in the NIH format and, after having it evaluated, defend it and answer general knowledge questions related to the proposal in an oral exam.

Chair, Committee to Formulate Guidelines for Faculty Tenure and Promotion in the Department of Biochemistry & Molecular Biology (1979-80)

Formulated the guidelines which were in continuous use for 15 years and were endorsed by five successive department chairmen.

Chair, Committee to Establish Criteria for Graduate Faculty Appointments and Approval to Chair Ph.D. Committees in Biochemistry & Molecular Biology (1985-87)

Formulated the criteria which were in continuous use for 10 years by the department and two of its chairmen.

Chair, Biology Sciences Ph.D. Steering Committee, UW-Milwaukee (1976)

Along with two other Zoology Department faculty and three Botany Department faculty, helped establish the Biological Sciences Ph.D. Program at UW-Milwaukee. Personally designed the poster for advertising the new Ph.D. Program, managed its production, and supervised the mailing of the posters to universities and colleges nationwide, which resulted in a large number of applications to the new program.

Chair, Committee that Formulated and Established Joint Graduate Studies between UW-Milwaukee and the Medical College of Wisconsin (1973-76)

A cooperative program was formulated by faculty from the two institutions and was formally established after being voted upon by each of the separate faculties. The program was a success and is still in existence. It expands and enhances the graduate studies of each institution.

Chair, Joint Course & Curriculum Committee between Zoology and Botany Departments, UW-Milwaukee (1973-74) and chief architect of a new interdisciplinary curriculum

With the collaboration of five other faculty (total of three from Zoology and three from Botany), joint courses were established in three areas of common interest: cell biology, genetics, and basic ecology. This new interdisciplinary curriculum was unanimously approved (with one abstention) by the faculty of both departments, which together numbered 36 members.

Other notable administrative service:

IRB (Institutional Review Board for the Protection of Human Subjects) - 1975-77.

IACUC (Institutional Animal Care and Use Committee) - 1984-88.

Faculty Senate - UW-Milwaukee, 1973-1975;

- Univ. of Oklahoma Health Sci. Ctr., 1991-94.

NIH, NIDDK - Extramural Program Senior Scientist (administrative consultant) in molecular biology - 1989, 1990. (A more detailed description follows.)

Administrative Experience at the National Institutes of Health
Senior Scientist, National Institutes of Health, 1989 - 1991

A. Position titles: Senior Scientist, Extramural Program

Div. of Kidney, Urologic & Hematologic Diseases (DKUHD) (Dr. Gary E. Striker, Director; Dr. David G. Badman, Asst. Director/Budget, Hematology Program Director) National Institute of Diabetes, and Digestive & and Kidney Diseases (NIDDK)

Senior Scientist (Guest Worker), Intramural Program
Laboratory of Chemical Biology (Dr. Alan N. Schechter, Chief; Dr. Patricia E. Berg, Senior Staff Fellow) NIDDK

B. Tour-of-duty: January 1, 1989 - December 31, 1990

C. Funding: Intergovernmental Personnel Act (IPA), 90% salary/FB

D. Duties: 50% Extramural/50% Intramural:

Extramural: DKUHD, NIDDK (Dr. Gary Striker, Director)

- (1) Asst. to Hematology Prgm. Director, Dr. David G. Badman.
 - (2) Wrote new Initiatives and recent Advances for the Division's Programs, which are part of each year's Implementation Plan that goes to Congress, for FY 1990 and FY 1991.
 - (3) Organized symposia and workshops in the areas of molecular and cellular biology of kidney and urologic diseases: a) NIDDK 40th Anniversary Symposium:
 - (a) "*Gene Regulation & Cellular Signaling in the Kidney & Urothelium*," March 7-9, 1990, at NIH, Bethesda, Maryland.
 - (b) Hands-on Workshop: "PCR Techniques" (didactic and laboratory), Howard Hughes/Mary Lasker Center, NIH, Oct. 19-21, 1990, Bethesda, Maryland.
 - (4) Study Sections, Program Representative:
Hematology I & II Study Sections. Molecular Physiology Study Section
 - (5) NIDDK National Advisory Council Program Representative
 - (6) Internal Review Panel, Small Business Innovative Research Grants SBIRs)
 - (7) Internal Review Panel, Conference Grants
- (Description of other duties available on request)

Intramural: Lab of Chem.Biol.,NIDDK (Dr. Alan Schechter, Chief)

Community Service (selected items)

Science Education, Elementary and Secondary Schools

Biology demonstrations/presentations

Milwaukee Public Schools, South Milwaukee Elementary, 6th grade	1974, 1975
Westminster Day School, Oklahoma City, elementary grades	1980-1984
Montgomery County, MD, public schools, Walter Johnson High School	1990
Oklahoma School of Science and Math, Oklahoma City (advanced high school)	1992

Mentor, Minority High School Students Summer

<u>Research Program</u> , University of Oklahoma College of Medicine (six students)	1986-1996
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Mentor, science fair projects

Junior high school (two students)	1981, 1984
Elementary school (two students)	1986, 1988

Judge, science fairs

Oklahoma City Public Schools	1985
Westminster Day School, Oklahoma City	1988

Adult Science Education (to the lay public)

<u>The Science Bag</u> , Milwaukee, Wisconsin (a public lecture, repeated each Friday for a month)	1977
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The Forum, First Unitarian Church, Oklahoma City (current topics for adults):

"Use of Animals in Biomedical Research" (with Gary White, D.V.M.)	Dec.,1991
"Diet and Longevity: A Fountain of Youth?" (with B. Connor Johnson, Ph.D.)	Apr.,1992
"Gene Therapy"	Dec.,1992
"The Human Genome Project"	Oct.,1993
"Human Cloning"	Apr.,1994

"DNA Fingerprinting"(w Jay Hanas,speaker)	May, 1995
"How to Make a Unicorn"	May, 1996
"Stem Cells"	Nov., 2000; Nov., 2002

Adult Science Education, public (continued)

Lay pulpit, First Unitarian Church, Oklahoma City
 Sermon title: "Fried Gene Tomatoes and the King James Bible" (On science and religion; conducted the full service) July,1995

Lay pulpit, First Unitarian Church
 Essay title: "For Love of a Frog" (On creativity) June,1996

Lay pulpit, First Unitarian Church
 Sermon title: "Hello, Dolly! To Clone or Not To Clone" July, 1998
 (Conducted service)

Lay pulpit, Unitarian Universalist Church of Lawton ,OK March, 1999
 Sermon: "Cloning Dolly: Facts, Future, Ethics"

Forum on the Future, Westminster Presbyterian Church, Oklahoma City (with Dr. Fred Silva, who was the featured speaker); a series of presentations about molecular biology, genes, human health, and ethics:

Jan.,1994	Jan. 28, 1996
Feb.,1994	Feb. 25, 1996
Mar.,1994	Mar. 31, 1996
Apr.,1994	Apr. 28, 1996
June, 1994	May 19, 1996
	June 30, 1996

Science and Religion Dialogue, Westminster Presbyterian Church; panel member/speaker Feb. 4, 1997

Science and Religion, II, Westminster Presbyterian Church; panel member/speaker Sept., 1998

Adult Leadership in Youth Programs

Unitarian Universalist Association

Substitute teacher (elementary grades), Church School, 1st Unitarian Church, Oklahoma City	1985
YRUU (Young Religious Unitarian Universalists), Career Choices Program, Co-Leader and Mentor, River Road Unitarian Church, Bethesda, MD	1990

Boy Scouts of America (fifteen years of service)

As a youth member and leader (ten years) - ScoWeGo

District, Buckskin Council (Eagle Scout, God and
Country Award, Silver Award [Explorer Scouts],
Emergency Service Explorer, AOA, Arrow of Light)

As an adult leader (five years) - Dan Beard District,

Last Frontier Council, Oklahoma City	
- Assistant Cub Master, Pack 4, Westminster Presbyterian Church	1984, 1985
- Cub Master, Pack 4, Westminster Presby- terian Church	1986, 1987
- Asst. Scoutmaster, Troop 240, Central Presbyterian Church	1986
- Committee Member, Troop 4, Westminster Presbyterian Church	1987, 1988
- Advancement Chairman, Troop 4	1988
- NESA (National Eagle Scout Association)	1987-1998

Charitable Contributions (yearly and periodic)

United Way; First Unitarian Church, Oklahoma City; Boy Scouts
of America; American Lung Association; Cystic Fibrosis
Foundation; March of Dimes; Disabled American Veterans;
Salvation Army; Goodwill Industries; Neighbor for Neighbor;
REST; Presbyterian Health Foundation.

PUBLICATIONS

1. Broyles, R. H., and Strittmatter, C. F. Hexose monophosphate shunt dehydrogenases during sea urchin development. Expt. Cell Res. **67**, 471-474 (1971).
2. Broyles, R. H., and Strittmatter, C. F. Hexose monophosphate shunt dehydrogenases in the developing frog. Compar. Bioc. Physiol. **44B**, 667-676 (1973).
3. Broyles, R. H., and Frieden, E. Sites of haemoglobin synthesis in amphibian tadpoles. Nature **241**, 207-209 (1973).
4. Broyles, R. H., and Deutsch, M. J. Differentiation of red blood cells in vitro. Science **190**, 471-473 (1975).
5. Deutsch, M. J., and Broyles, R. H. Effect of phenylhydrazine on the multiple hemoglobins of Rana catesbeiana tadpoles. Devel. Biol. **46**, 277-231 (1975).
6. Broyles, R. H., and Strittmatter, C. F. Hexose monophosphate shunt dehydrogenases in the sea urchin and the frog: Comparison of some functional properties of the enzymes in vitro. Compar. Bioc. Physiol. **57B**, 249-255 (1977).
7. Broyles, R.H. Hormones. In Laboratory Manual for Animal Biology, D. B. Mooren, ed., Kendall, Hunt Publ. Co., Dubuque, Iowa, pp. 87-89 (all editions, 1974-1977).
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Abstracts of Oral and Poster Presentations

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32. **Broyles, R.H.**, Palmer, J.C., Ramseyer, L.T.H., Smith, D.J., Jarman, R.N., Do, T.H., and McBride, K.A. Developmental regulation of globin gene expression: Hemoglobin and globin mRNA switching in heterospecific erythroid cell hybrids. (Minisymposium talk presented at the Mid-America Molecular Biology Colloquium, organized by the Dept. of Biochemistry & Molecular Biology, College of Medicine, Univ. of Oklahoma at Oklahoma City; Shangri-La Resort, Afton, Oklahoma, Oct. 14 through 17, 1986.)
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48. **Broyles, R.H.** Developmental signaling: Factors that program and trans-regulate globin genes. (Invited oral presentation at the **Oklahoma Biomedical Research Symposium sponsored by the Presbyterian Health Foundation**, the University of Oklahoma Health Sciences Center, and the Oklahoma Medical Research Foundation; held at the Waterford Hotel and the Univ. of Oklahoma Health Sciences Center, Oklahoma City, February 21-23, 1988.)
49. **Broyles, R.H.** Developmental regulation of gene expression: Globin switching as a model. (Oral presentation delivered, by invitation, to extramural and intramural scientists at the **National Institutes of Health, Bethesda, Maryland**, March 16, 1988.)
50. Barker-Harrel, J., McBride, K.A., and **Broyles, R.H.** Two chemical methods of cell fusion for efficient formation of erythroid heterokaryons. (Presented at the 6th Conference on Hemoglobin Switching, co-sponsored by NIH and the Univ. of Washington, Seattle; Airlie House, VA, Sept. 24-27, 1988.)
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54. **Broyles, R.H.** "Developmental Regulation of Globin Genes in Erythroid Heterokaryons." (Seminar presented at The Johns Hopkins University School of Medicine, Hematology "Soup Seminar," Feb. 28, 1989.)
55. **Broyles, R.H.** "Globin Gene Regulation During Development." (A pair of lectures presented at the University of Kansas Medical Center, April 13 & 14, 1989, as a 1988-89 MASUA Honor Lecturer.)
56. Barker-Harrel, J., Ramseyer, L.T.H., Smith, D.J., and **Broyles, R.H.** Cell fusion mediated delivery of trans factors for hemoglobin switching. (Presented at the Gordon Research Conference on Red Cells, Plymouth, NH, Aug. 7-11, 1989.)
57. **Broyles, R.H.** "The Cellular and Molecular Biology of Developmental Hemoglobin Switching." (An invited lecture presented in honor of Dr. C.F. Strittmatter, IV, Odus M. Mull Professor of Biochemistry, on his retirement, October 12, 1989.)
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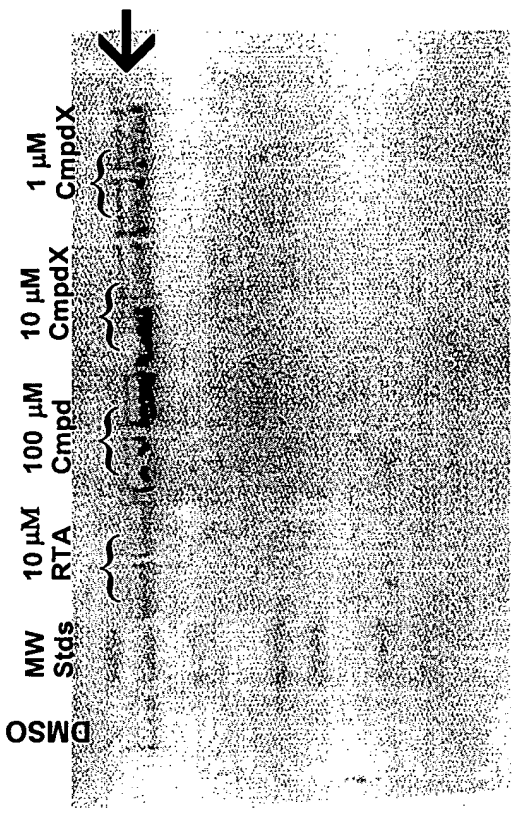
human β -globin gene that binds a conserved CAGTGC motif, is bound to the repressed β -globin promoter in vivo in K562 cells and specifically binds an analogous site in the mouse β^{Major} -globin promoter. (*Presented at the 46th annual meeting of the Amer.Soc.Hematology, San Diego, CA, Dec. 4-7, 2004.*) ***Blood* 104**:345-346a (2004).

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Induction of Fth in Differentiating NT- 2 Human Embryonal Carcinoma Stem Cells



NT 2 (*NTERA-2*) cells differentiating into neurons in spheres as a result of retinoic acid (RTA) treatment.



Western blot with antiFth specific anti serum of lysates of NT 2 cells treated with inducing/differentiating agents in the medium for 8 days. Arrow: Bands of polymerized ferritin heavy chains (Fth).

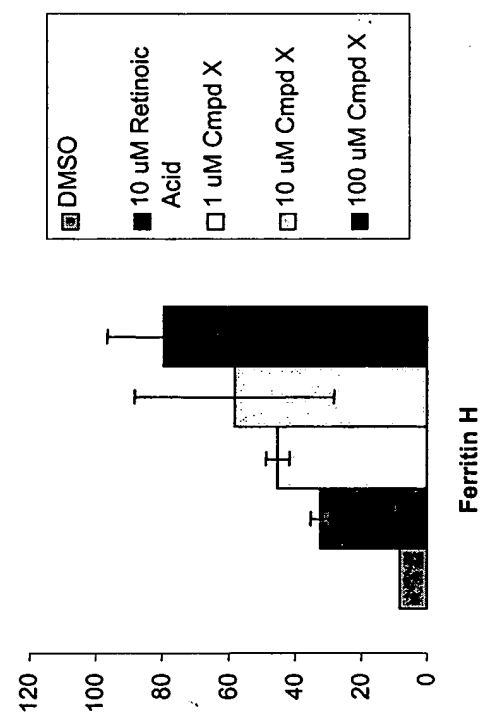
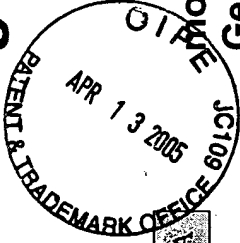


FIG. A

FtH Represses β^{Major} -Globin *In vivo* in Transgenic (FtH) Mice



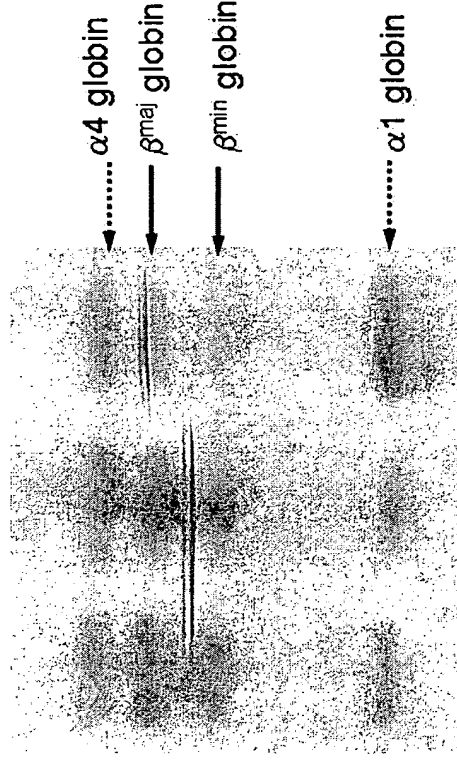
FtH represses the
transgenic mouse β^{Major} Globin
Gene in Transgenic Mice.

(a) Schematic diagram of the human FtH construct used for creation of ferritin transgenics. (b) UT Page electrophoresis of globin chains from an FtH transgenic mouse (lane 1), a non-transgenic mouse (lane 2), and globin standards (lane 3). (c) Blood smears from a non-transgenic mouse (wt) and a transgenic mouse (FtH transgenic). The FtH-Tg mice appear to have a mild β -thalassemia characterized by increased numbers of target cells (arrow) indicative of inclusions due to precipitated excess α -chains.



β^{Maj}/β^{Min} : 1.37 1.56

1 2 3



% Target
Cells:

wt 6.5% FH transgenic 22.6%

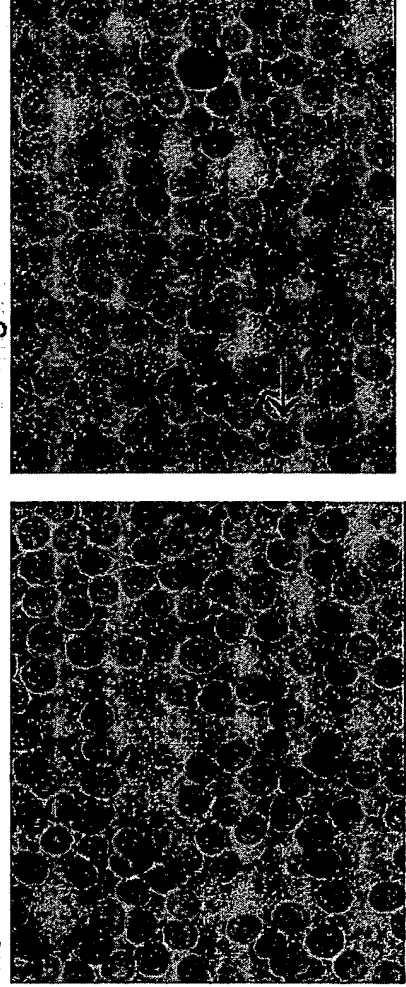


FIG. B